Application No.: 10/506,630 Docket No.: 300622004601

CLAIM AMENDMENTS

1-32. (canceled)

33. (new): A hybrid formed from formed from a non-ribosomal peptide synthase (NRPS) and a modular polyketide synthase (PKS) said hybrid comprising at least an NRPS domain and at least a PKS extender module.

wherein said NRPS domain is defined as consisting of the amino acid sequence from the N-terminus of an adenylation (A) domain through the C-terminus of a peptidyl carrier protein (PCP) domain; and

wherein said PKS extender module is defined as consisting of the amino acid sequence from the N-terminus of a ketosynthase (KS) domain through the C-terminus of an acyl transferase protein (ACP) domain;

wherein the C-terminus of said NRPS domain is covalently linked to the N-terminus of a intra-molecular linker (RAL) and the N-terminus of the PKS extender module is covalently linked to the C-terminus of said RAL:

wherein said RAL is defined as the amino acid sequence between the C-terminus of an upstream ACP domain and the N-terminus of an adjacent downstream KS domain; said ACP and KS domains occupying adjacent modules in the same reading frame; and

wherein said NRPS domain does not natively interact with any PKS protein;

whereby the RAL effects the transfer of a polypeptide chain from said first module to said PKS module.

- 34. (new): The hybrid of claim 33, wherein said RAL is selected from the group consisting of M2 *ery*, M4 *ery*, M6 *ery*, M2 *rif*, M2 *rif*, M5 *rif*, M3 *rap*, M4 *rap*, and M7 *rap* intrapolypeptide linkers (SEQ ID NO's: 18-26, respectively).
- 35. (new): The hybrid of claim 33, wherein said first module comprises the PCP domain of NovH and said second module comprises the KS domain selected from the group consisting of ery module 2 and 6.

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36. (new): A hybrid formed from formed from a non-ribosomal peptide synthase (NRPS) and a modular polyketide synthase (PKS) said hybrid comprising at least an NRPS domain and at least a PKS extender module.

wherein said NRPS domain is defined as consisting of the amino acid sequence from the N-terminus of an adenylation (A) domain through the C-terminus of a peptidyl carrier protein (PCP) domain; and

wherein said PKS extender module is defined as consisting of the amino acid sequence from the N-terminus of a ketosynthase (KS) domain through the C-terminus of an acyl transferase protein (ACP) domain;

wherein the C-terminus of said NRPS domain is covalently linked to the N-terminus of a inter-molecular linker (ERL) and the N-terminus of the PKS extender module is covalently linked to the C-terminus of said ERL, and

wherein said ERL is defined as a contiguous polypeptide comprising, in order, (1) the amino acid sequence beginning at the C-terminus of the ACP domain of the most downstream module of a first open reading frame and (2) the amino acid sequence upstream of the N-terminus of the most upstream KS domain of a second open reading frame, which second open reading frame is immediately adjacent to and downstream of said first open reading frame; and

wherein said NRPS domain does not natively interact with any PKS protein;

whereby the ERL effects the transfer of a polypeptide chain from said first module to said second module.

- 37. (new): The hybrid of claim 33, wherein the ERL is selected from the group consisting of M3 *ery*, M5 *ery*, M4 *rif*, M7 *rif*, M8 *rif*, M9 *rif*, M5 *rap*, and M11 *rap* interpolypeptide linkers (SEQ ID NO's: 27-34, respectively).
- 38. (new): The hybrid of claim 36, wherein said first module comprises the PCP domain of NovH and said second module comprises the KS domain selected from the group consisting of *ery* module 2 and 6.

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 (new): A method to prepare a polypeptide-polyketide which comprises culturing cells containing the hybrid of claim 33.

40. (new): A method to prepare a polypeptide-polyketide which comprises culturing cells containing the hybrid of claim 36.

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